Armed Forces College of Medicine

AFCM

Biochemistry of vision (Vitamin A)

By Dr. Amal El-Shal
Professor of Medical Biochemistry & Molecular Biology

Lecture Key points

1. Vitamins classification according to their solubility and functions
2. Comparison between fat and water soluble vitamins
3. Different forms and functions of vitamin A & its role in visual cycle
4. Vitamin A deficiency clinical disorders

INTENDED LEARNING OBJECTIVES (ILO)

By the end of this lecture the student will be able to:

1. Classify vitamins according to their solubility and functions
2. Compare between fat and water soluble vitamins
3. Distinguish different forms and functions of vitamin A
4. Interpret the role of vitamin A with illustration in visual cycle
5. Correlate vitamin A deficiency to its clinical disorder

Case scenario

24 years old man presents to clinician with bad ,foul ,odor, greasy stool after fatty meal intake. Also he can't move at dim night. Past history revealed repeated respiratory tract infection. Stool examination demonstrated increase fat content.

What is your provisional diagnosis?
Vitamin A deficiency
Because of night blindness

Vitamins

- Vitamins are **organic nutrients** that are required to **small quantities** for a variety of biochemical functions.
- They **cannot be synthesized** by the body in adequate amounts
- and must therefore be supplied in diet
- They are **necessary to maintain good health**
- Absence or relative **deficiency** of vitamins in diet leads to characteristic deficiency states and **diseases**.

So they must present in diet

Classification of the vitamins

Vitamins fall into 2 classes according to their solubility, fat soluble and water soluble

- **Vitamins**
  - **Water soluble**
    - **Non-B complex**
      - Ascorbic acid (vitamin C)
    - **B Complex**
      - **Energy releasing**
        - Thiamine (vitamin B_1)
        - Riboflavin (vitamin B_2)
        - Niacin (vitamin B_3)
        - Biotin
        - Pantothenic acid
      - **Hematopoietic**
        - Folic acid
        - Vitamin B_{12}
      - **Other**
        - Pyridoxine (vitamin B_6)
        - Pyridoxal
        - Pyridoxamine
  - **Fat soluble**
    - Vitamin A (retinol, β-carotenes)
    - Vitamin D (cholecalciferol)
    - Vitamin K (phylloquinones, menaquinones)
    - Vitamin E (tocopherols)

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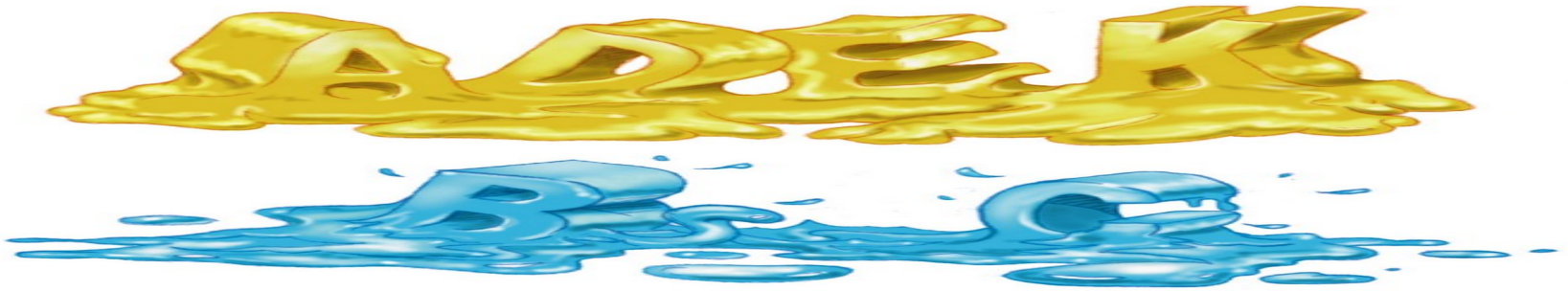


Fat Soluble Vitamins vs. Water Soluble Vitamins

According to solubility, vitamins are classified into water-soluble and lipid-soluble vitamins

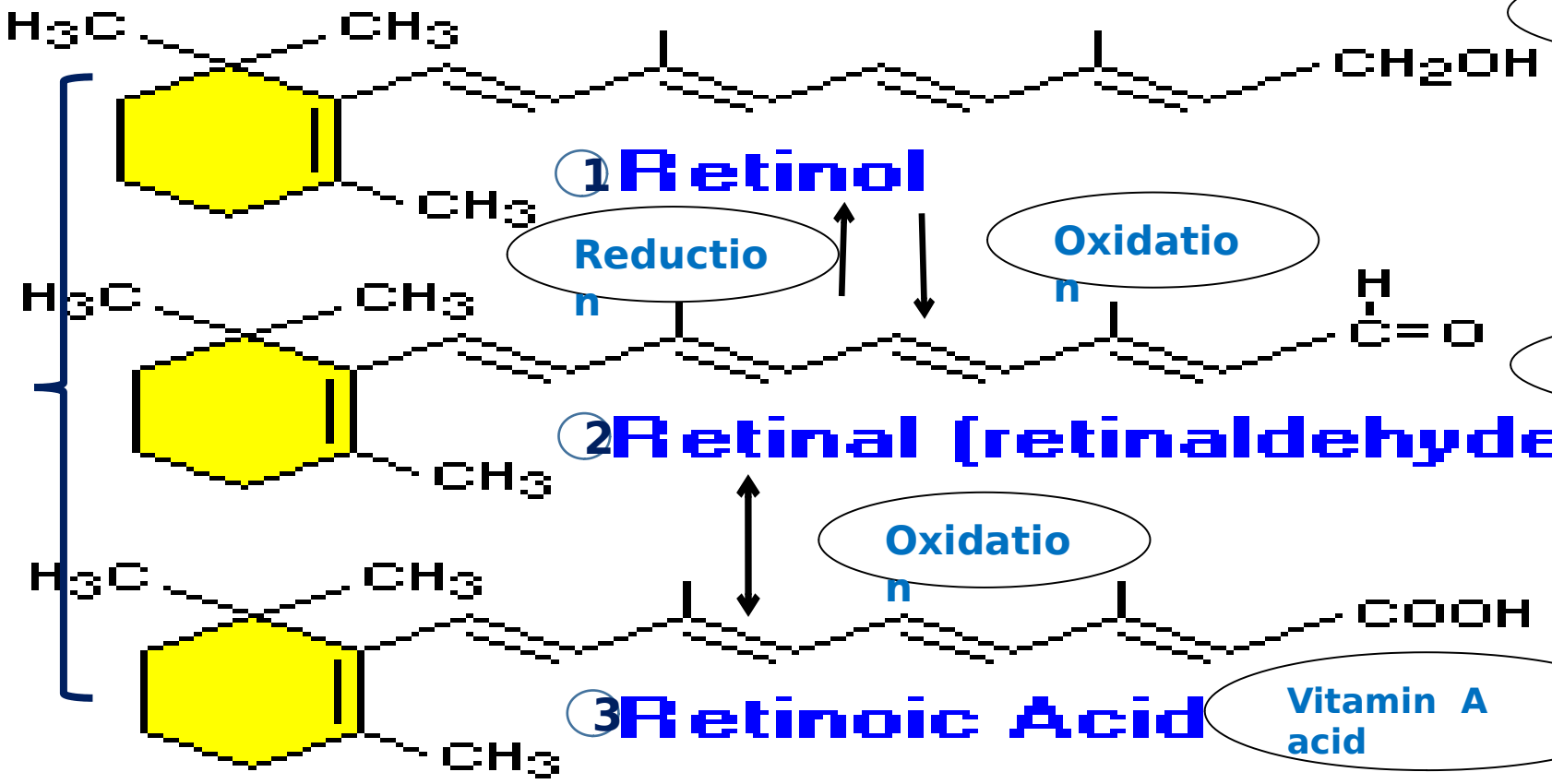
	Water-Soluble Vitamins	Lipid-Soluble Vitamins
	Vitamin C Vitamin B (8 members)	Vitamins A, D, K, and E
Intestinal absorption	Vitamin B12 needs a specific glycoprotein (intrinsic factor)	- Need bile acids - Affected by biliary obstruction
Transport in blood	May have specific transporter (e.g. transcobalamine for B12)	By lipoproteins and/or by Specific transport proteins
Urinary excretion	excreted once their concentration exceeds the renal threshold	Not excreted because insoluble in water
Storage in human body	No storage (Vitamin B12 is an exception)	Stored mainly in the liver
Toxicity due to excess intake	No toxicity	Toxicity occurs (Vitamin E is an exception)
Coenzyme function	Form coenzymes necessary for energy production or for hematopoiesis	Only vitamin K has coenzyme function

Vitamin A (Antinight blindness) (Antixerophthalmia)

Vitamin A (Antinight blindness)(Antixerophthalm)

Forms of vitamin (Retenoids) :

A-In animals



n Plant sources : Carotenes

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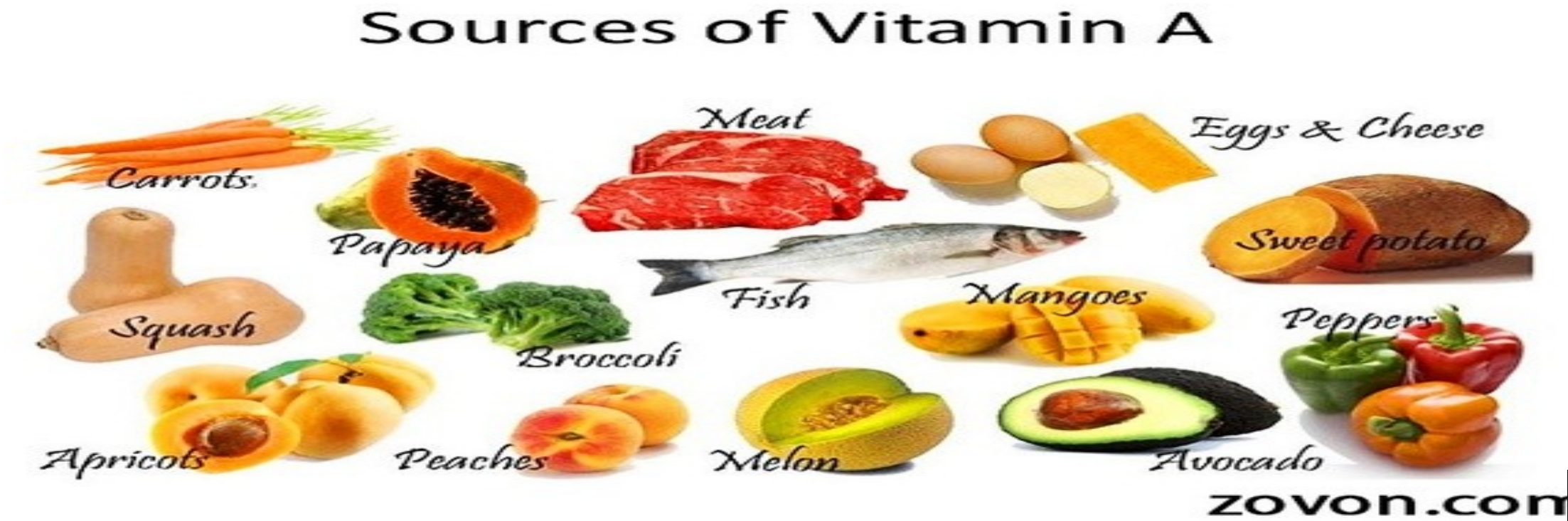
Dietary sources of vitamin A

Sources:

- **Plants** : pigmented vegetables and fruits (**Carotenes**) .
- **Animals** : liver , egg volk , fish liver oil and milk



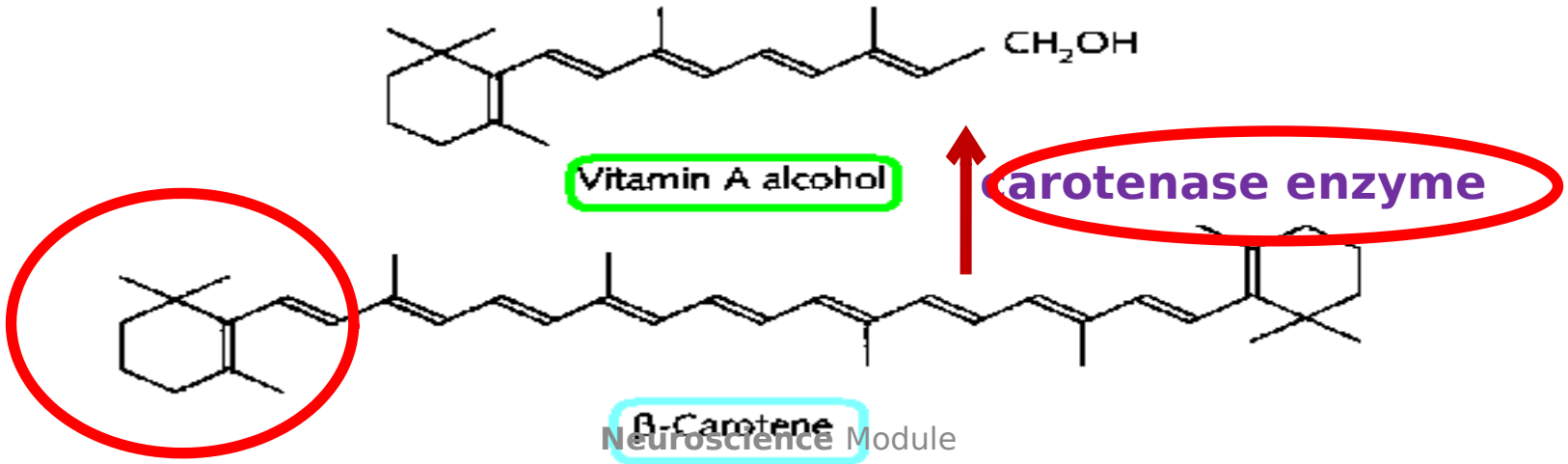
Provitamin A Carotenes (α, β, γ)

Chemically :

❖ **Vitamin A is a polyisoprenoid compound attached to β-ionone ring which is essential for its activity.**

❖**Carotenes (α, β, γ): are provitamin A . they are yellow orange pigments in plants.**

❖**They are inactive precursors, β- carotene is cleaved in the liver by carotenase enzyme (oxidation) to produce 2 molecules of retinal, that converts to retinol by reduction .**



Absorption and transport of vitamin A

a) Retinol is present in animal food as an ester which is then hydrolyzed in the intestinal mucosa to give retinol and free fatty acid.

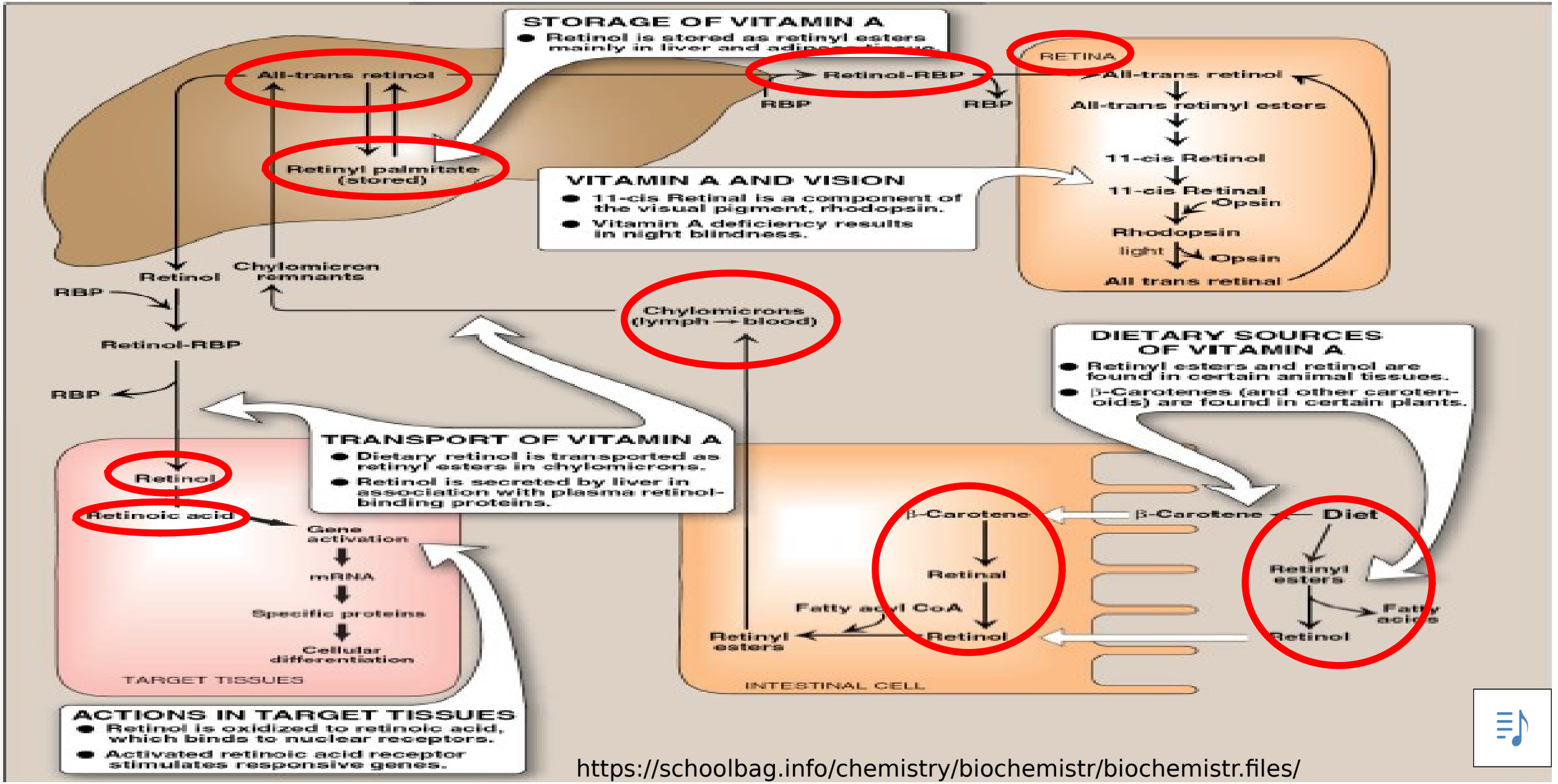
b) Retinol can also obtained from β-carotene in plants as mentioned .

c) Retinol is reesterified in mucosal cells and absorbed (by the help of bile salts) and is secreted in chylomicrons and taken and stored by the liver (95%), as retinyl palmitate (an ester), bind to cellular retinol-binding protein (RBP) .

d) When needed, this ester is hydrolyzed to give the alcohol form (retinol) which is transported in the blood bound to retinol-binding protein (RBP) to the peripheral tissues . RBP is synthesized by liver. Retinoic acid transported in plasma bounded to albumin.

e) RBP complex is attached to specific cell surface receptor of peripheral cells such as retina, gonads, to help entry of retinol inside leaving the carrier protein outside.

Absorption and transport of vitamin A



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Retinoids (Vitamin A) have the following functions

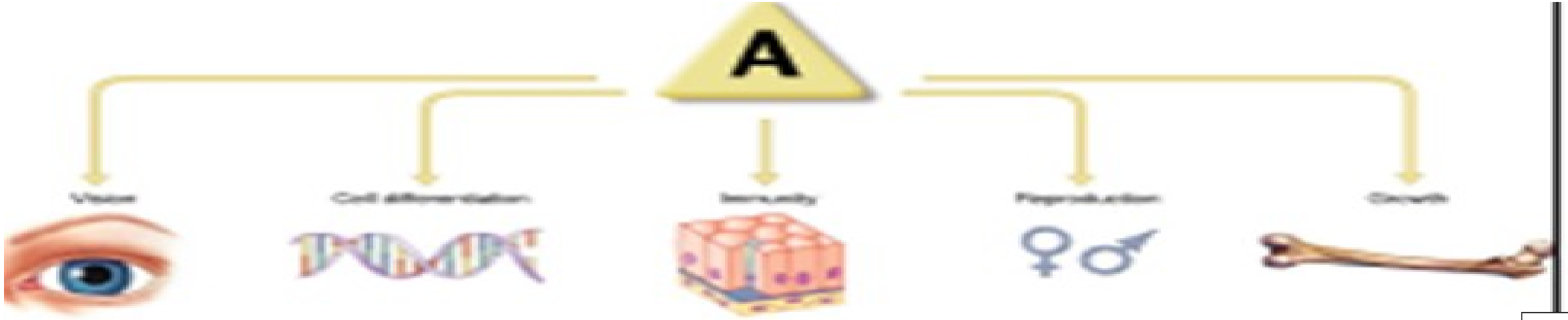
a) Retinal → normal vision.

b) Retinol → normal reproduction .

c) Retinoic acid → normal growth & differentiation of epithelial tissue and mucus secretion → supports the body's barrier against infections &

defense against pathogens(if decrease → recurrent infections).

d) β-carotenes → antioxidants.



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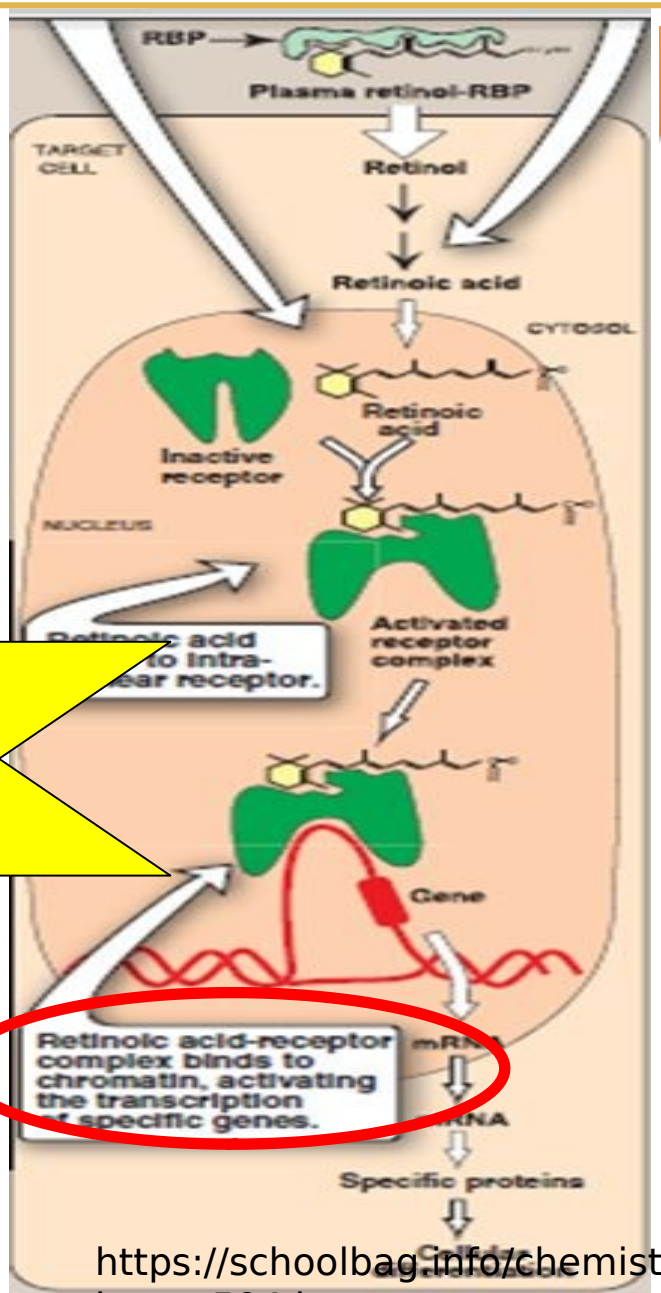
Mechanism of action of vitamin A

Production of specific proteins that mediate several physiologic functions.

For example, vitamin A control the keratin gene expression through controlling transcription of the gene in epi tissues of the body tre

Explain on a biochemical basis? vitamin A used in treatment of psoriasis



Mechanism of action of Vitamin A

RBP-Retinol complex goes to extra-hepatic tissues- Retina, skin, gonads and other tissues

↓

Transport protein on cell surface carries retinol

↓

Retinol oxidized → Retinoic acid

↓

Binds to specific receptor proteins (Retinoic acid receptors RAR) present in the nucleus

↓

Bind to HRE (Hormone receptor elements) on DNA

↓

Retinoid –specific RNA synthesis

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”Role of Vitamin A in vision" visual cycle

- The retina contains **two types of photoreceptors**, which are photosensitive to light ; Rods and cones.
- **Rods** have a visual pigment "**rhodopsin**" essential for vision in dim light . (**Rhodopsin = cis-retinal + opsin**) .
- **Cones,** have a visual pigment " **Iodopsin** " essential for color vision in bright light.
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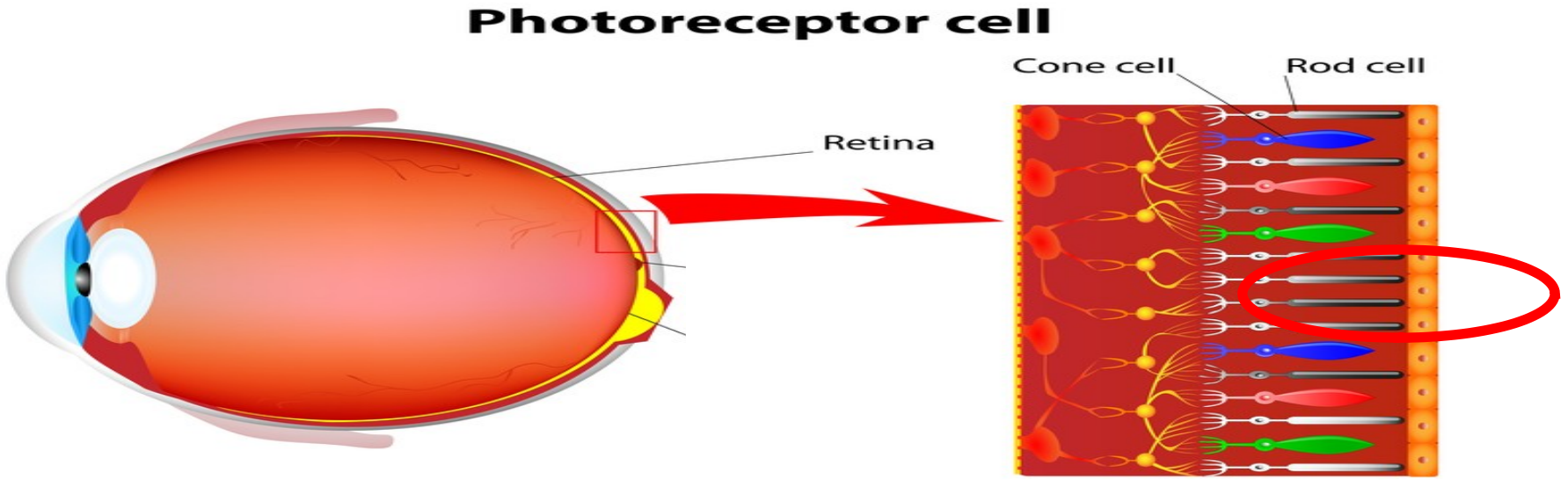

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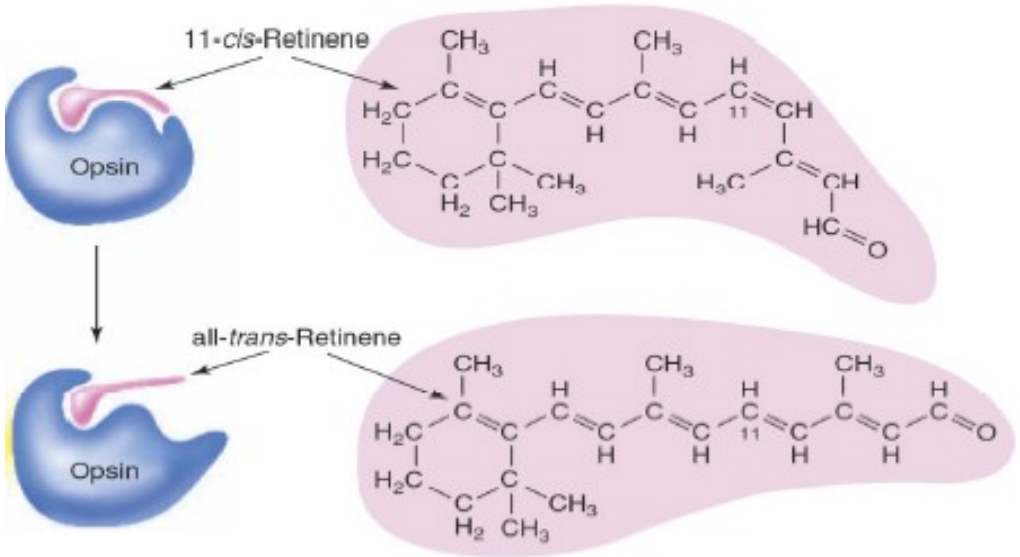
Retinal can exist in two possible configurations (shapes)

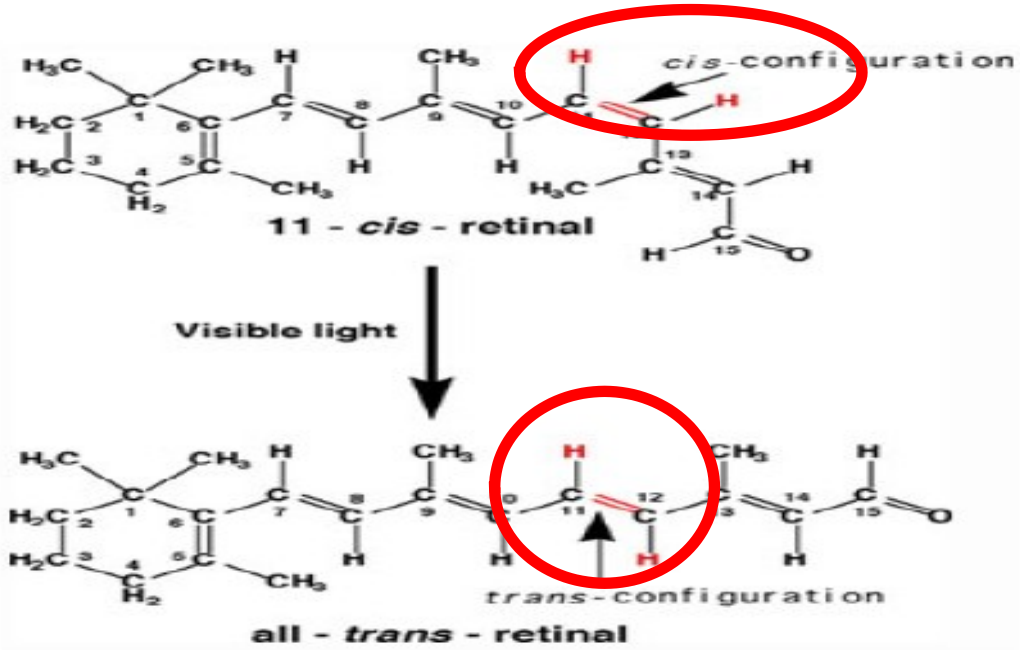
11-cis isomer

the hydrogens are on the same side of the double bond between carbon atom 11 and carbon atom 12

11-trans isomer

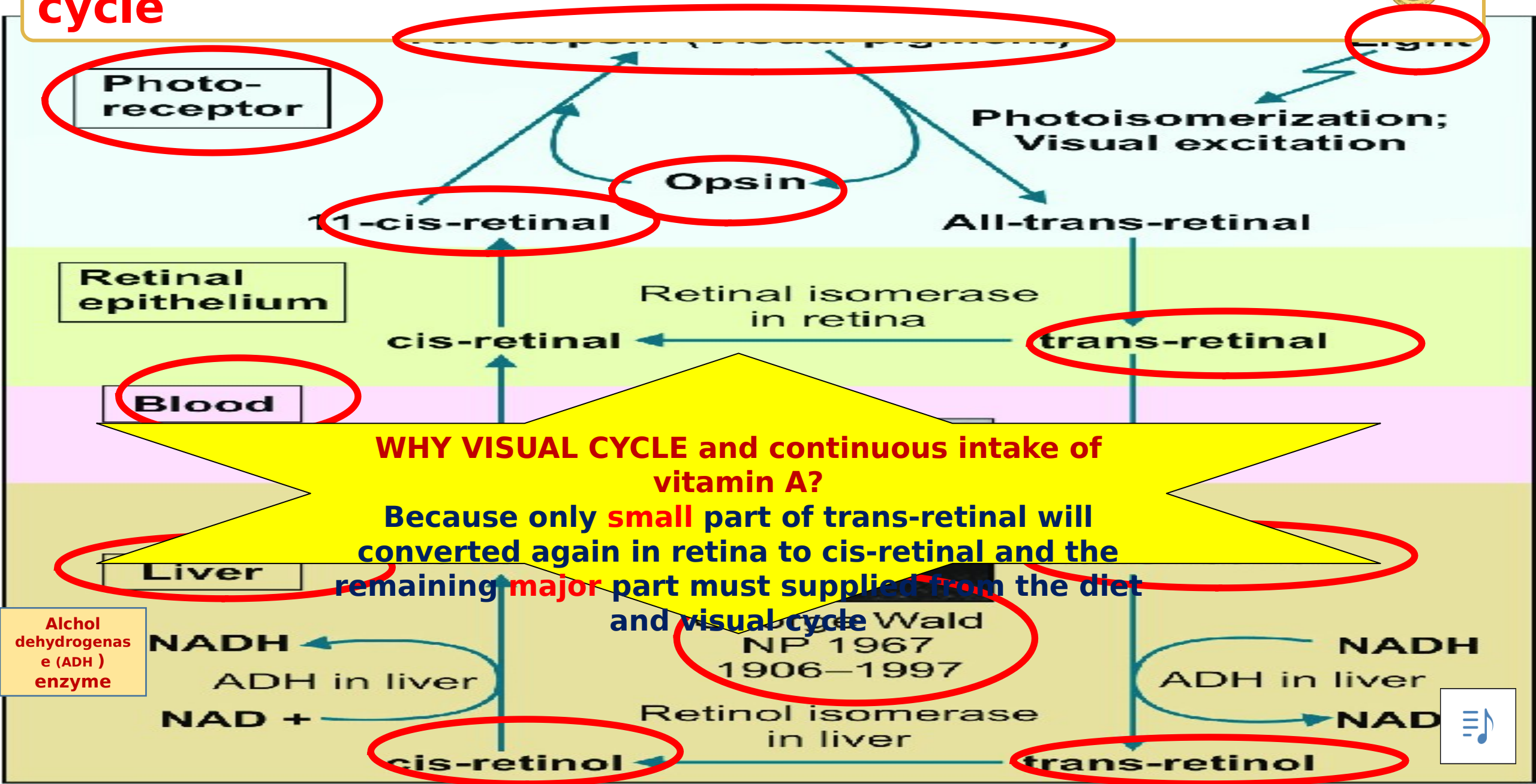
the hydrogens are on the opposite side of the double bond between carbon atom 11 and carbon atom 12





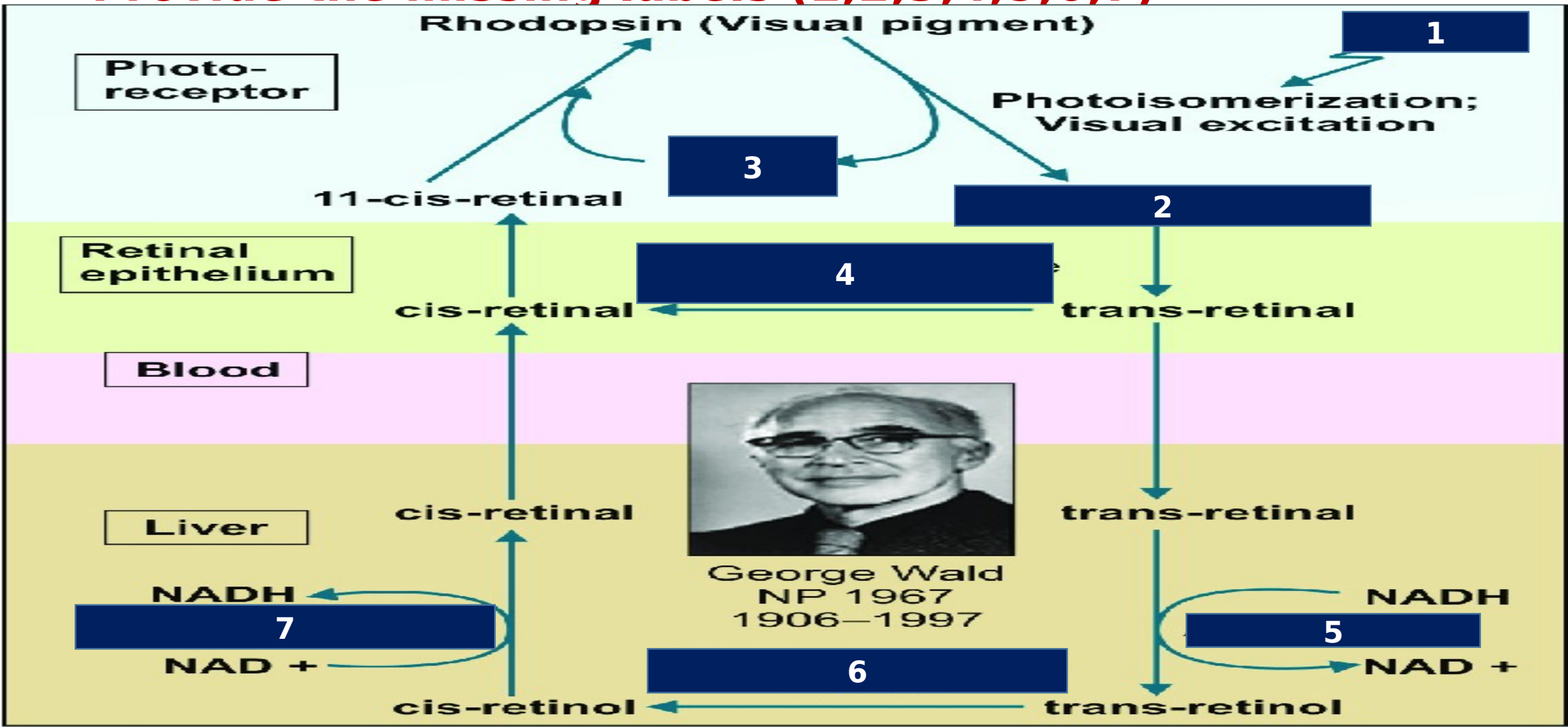
NB. ***The all-trans form is more stable, but only the 11-cis form is found attached to opsin.***

Role of Vitamin A in vision: visual cycle ; Wald's visual cycle

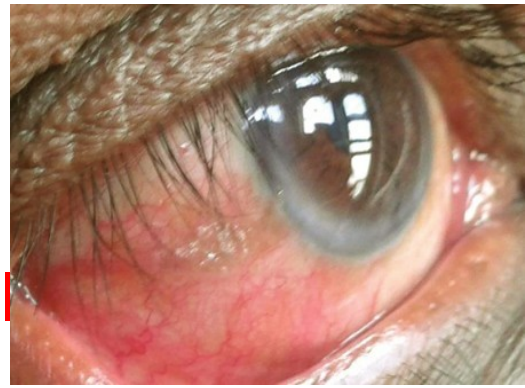


Role of Vitamin A in visual cycle (Wald's visual cycle) Quiz

Provide the missing labels (1,2,3,4,5,6,7)



Manifestations of Vitamin A deficiency



1. Manifestations in the eye:

i- Earliest symptoms :Night blindness (Nyctalopia):

Visual acuity is diminished in dim light but normal in day l

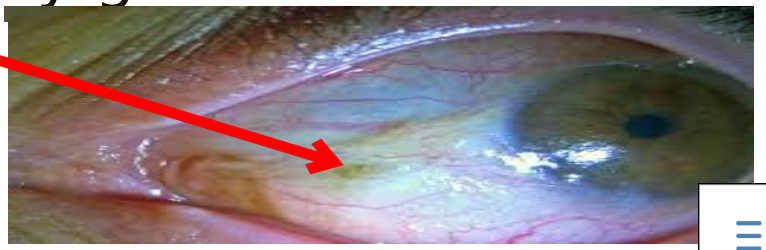
ii- Xerophthalmia:

The conjunctiva becomes dry(sandy sensation & irritation), thick and wrinkled.

iii- Bitot spots: These are seen as grayish white triangular plaques firmly adherent to conjunctiva.

IV Keratomalacia (softening of the cornea):

Degeneration of the corneal epithelium which may get vascularized.



2-Skin and mucous membrane:

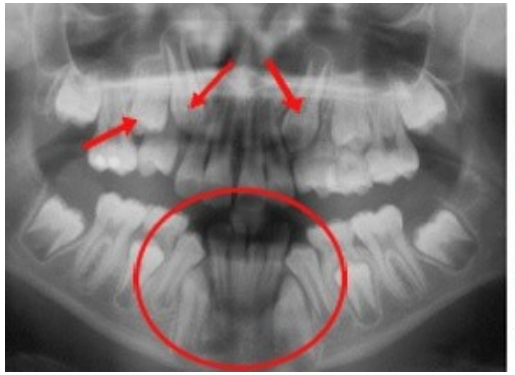
- **Follicular hyperkeratosis**

The skin becomes rough, dry and scaly (xerosis cutis); due to hyper-keratinization of epithelium lining the follicles. .

- **Epithelium of the respiratory Tract, Gastrointestinal Tract, Genitourinary tract :**

reduced mucous secretion, dryness, and susceptibility to bacterial invasion.

3-Delayed growth of bones and eruption of teeth



Clinical indications of Vitamin A

- 1-Dietary deficiency & defective absorption (absence of bile).
- 2-Topical vitamin A (tretinoin) used in treatment of Acne & psoriasis (Dermatologic problems) due to its effect on epithelial tissue and on glands (control gro
- 3-Skin aging and wrinkles are treated with of tretinoin (all-trans retinoic acid)
- 4-Chronic infection as respiratory tract infe
- Isotretinoin is teratogenic not used in preg

Pregnant women particularly should not ingest (eat) excessive quantities of vitamin A or take because of its potential for teratogenesis (causing congenital malformations in the developing fetus Also no treatment with vitamin A during pregnancy.

Vitamin A clinical indications quiz (USMLE)

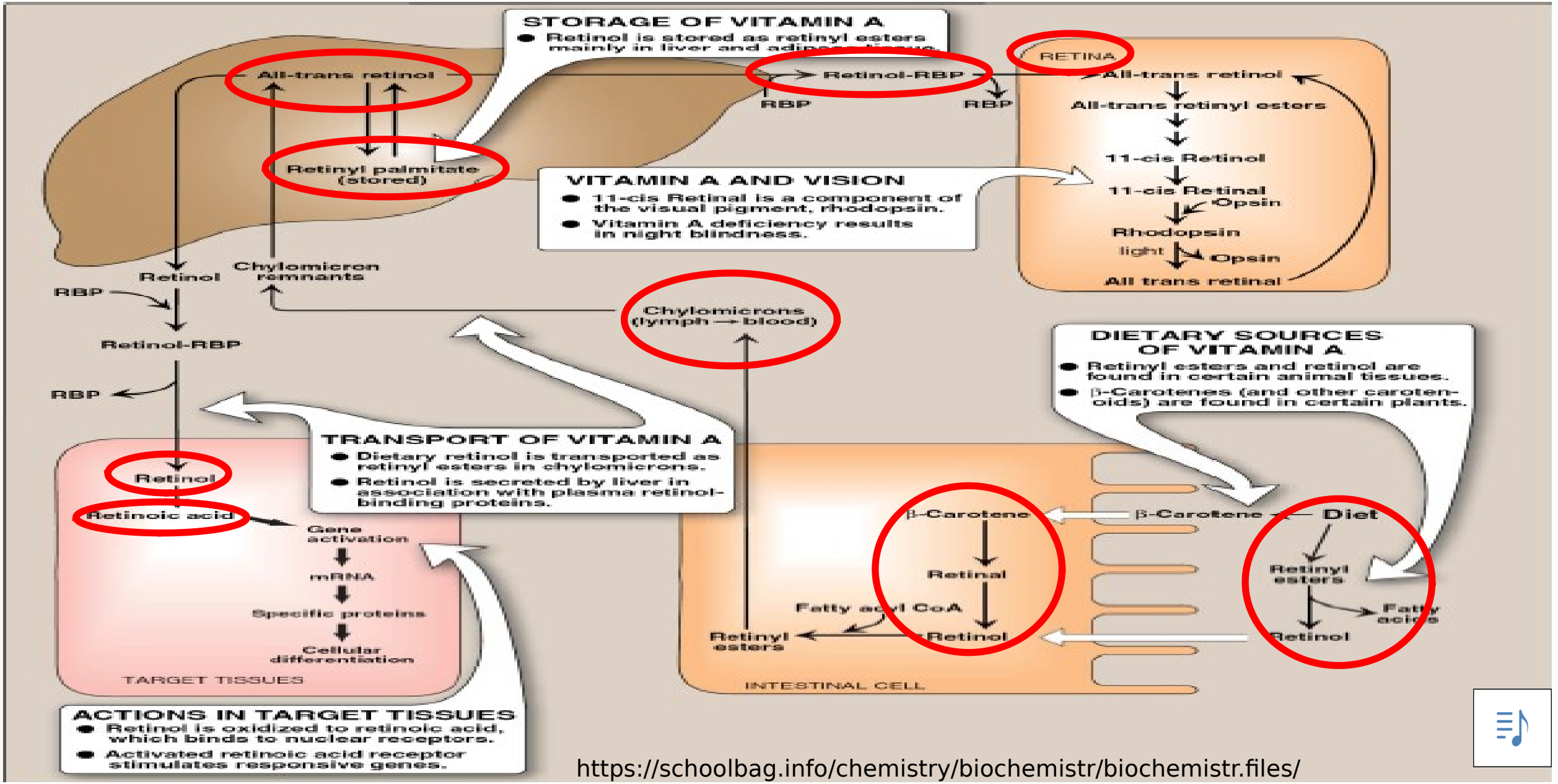
One of the following vitamins is useful in treatment of acne:

A. Vitamin D
B. Vitamin K
C. Vitamin B9
D. Vitamin B12
E. Vitamin A

Lecture Summary

1. **Comparison between fat and water soluble vitamins**
2. **Different forms and functions of vitamin A & its role in visual cycle**
3. **Vitamin A deficiency clinical disorders**

Summary of vitamin A metabolism



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SUGGESTED TEXTBOOKS

- "Lippincott's Illustrated Reviews in Biochemistry" by P.C.Champe, R.A.Harvey and D.R.Ferrier
- "Harper's Biochemistry" by R.K.Murray, D.K.Granner, P.A. Mayes and V.W.Rodwell.
- Fundamentals of Clinical Chemistry (Tietz) Sixth
- "Textbook of Biochemistry with Clinical Correlations" by T.M.Devlin
- ***www.namrata.co- Biochemistry for medics***

Dr. Amal El-Shal